ANSWER 3 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:186710 CAPLUS
DOCUMENT NUMBER: 124:278432
TITLE: Inflammatory and immunological parameters of disease activity in rheumatoid arthritis patients treated with minocycline
AUTHOR(S): Kloppenburg, Margreet; Dijkmans, Ben A. C.; Verweij, Cor L.; Breedveld, Ferdinand C.
CORPORATE SOURCE: Department of Rheumatology, Leiden University Hospital, Building 1, C4-R, P.O. Box 9600, RC Leiden, 2300, Neth.
SOURCE: Immunopharmacology (1996), 31(2-3), 163-9
CODEN: IMMUDP; ISSN: 0162-3109
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The objective of this study was to analyze the anti-inflammatory effect of minocycline in rheumatoid arthritis. Serum samples of 65 RA patients who completed a 26-wk randomized double-blind trial of minocycline (100 mg twice a day) vs. placebo were studied. In this trial some clin. parameters and, in particular, the acute-phase response decreased significantly in the minocycline-treated group. Serum levels of albumin and interleukin-6 (IL-6) were compared with CRP levels in order to study the acute-phase response. Furthermore, rheumatoid factor (RF) and total Ig isotypes as well as serum levels of soluble interleukin-2 receptor (sIL2-2R) were determined in order to study immunol. parameters of the disease. Igs and cytokines were measured by ELISA. Serum levels of albumin remained stable, whereas serum CRP levels decreased both in the minocycline- and in the placebo-treated group. Serum levels of IL-6 decreased in the minocycline-treated group only and this decrease was pos. correlated with the decrease in CRP levels. Minocycline significantly decreased serum IgM-RF, IgA-RF, total IgM and total IgA levels. In addition the ratio of IgM-RF/total IgM decreased in the minocycline-treated group. No such changes were observed in the placebo-treated group. The anti-inflammatory effect of minocycline in RA patients may be due to the reduction in the synthesis of IL-6 and rheumatoid factor.

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ANSWER 11 OF 38 USPATFULL on STN
ACCESSION NUMBER: 2003:159805 USPATFULL
TITLE: Diagnostic markers of acute coronary syndrome and methods of use thereof
INVENTOR(S): Valkirs, Gunars, Escondido, CA, UNITED STATES
Dahlen, Jeffrey, San Diego, CA, UNITED STATES
Buechler, Kenneth F., Rancho Santa Fe, CA, UNITED STATES
Kirchick, Howard J., San Diego, CA, UNITED STATES
PATENT ASSIGNEE(S): Biosite, Inc. (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003109420	A1	20030612	<--
APPLICATION INFO.:	US 2002-139086	A1	20020504	(10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-288871P	20010504 (60)
	US 2001-315642P	20010828 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: FOLEY & LARDNER, P.O. BOX 80278, SAN DIEGO, CA, 92138-0278
NUMBER OF CLAIMS: 68
EXEMPLARY CLAIM: 1
LINE COUNT: 4194
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to methods for the diagnosis and evaluation of acute coronary syndromes. In particular, patient test samples are analyzed for the presence and amount of members of a panel of markers comprising one or more specific markers for myocardial injury and one or more non-specific markers for myocardial injury. A variety of markers are disclosed for assembling a panel of markers for such diagnosis and evaluation. In various aspects, the invention provides methods for the early detection and differentiation of stable angina, unstable angina, and myocardial infarction. Invention methods provide rapid, sensitive and specific assays that can greatly increase the number of patients that can receive beneficial treatment and therapy, reduce the costs associated with incorrect diagnosis, and provide important information about the prognosis of the patient.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 2003109420 A1 20030612 <--
SUMM [0004] ACS is a manifestation of vascular injury to the heart, also referred to as myocardial injury or myocardial damage, that is commonly secondary to atherosclerosis or hypertension, and is the leading cause of death in the United States. ACS is commonly caused by occlusion associated with coronary artery disease cause by atherosclerotic plaque formation and progression to either further occlusion or fissure. ACS can be

Sensitivity and specificity of. . .

DETD [0191] The observation that MMP-9, cTnI, BNP, and CRP are each independently associated with 10-month patient mortality indicates that multi-marker testing strategies in patients with suspected ACS can advantageously. . . therapies to different underlying pathophysiologic mechanisms. This "risk profile" may be determined by various combinations of MMP-9, cTnI, BNP, and CRP, as well as by other markers used in addition to or substituted for said markers.

DETD [0192] Additionally, markers such as MMP-9 that play a direct pathogenic role in atherosclerosis and its complications can provide novel therapeutic targets for drug discovery. For example, the MMP system might be regulated on. . . proenzyme activation, and inhibition by tissue inhibitors of metalloproteinases (TIMPs). Modification of one or more of these steps may prevent atherosclerotic plaque rupture and modify adverse vascular and cardiac remodeling.

DETD . . . composition directed to MMP-9 or a fragment thereof); and/or delivery of small molecule thrapeutics (e.g., heparin can decrease MMP-9 synthesis, tetracycline antibiotics can inactivate MMPs by chelating zinc, and HMG Co-A Reductase inhibitors and activators of Peroxisomal Proliferator-Activator Receptor (PPAR)-gamma can. . .

CLM What is claimed is:

. . . are selected from the group consisting of an MMP-9 level, a TpP level, an MCP-1 level, an H-FABP level, a CRP level, a creatine kinase level, an MB isoenzyme level, a cardiac troponin I level, a cardiac troponin T level, and a level of complexes comprising cardiac troponin I and cardiac troponin T.

. . . wherein said specific marker for myocardial injury is selected from the group consisting of annexin V, B-type natriuretic peptide, β-enolase, cardiac troponin I, creatine kinase-MB, glycogen phosphorylase-BB, heart-type fatty acid binding protein, phosphoglyceric acid mutase-MB, and S-100ao.

. . . to claim 41, wherein said non-specific marker for myocardial injury is selected from the group consisting of a marker of atherosclerotic plaque rupture, a marker of coagulation, C-reactive protein, caspase-3, hemoglobin α.sub.2, human lipocalin-type prostaglandin D synthase, interleukin-1β, interleukin-1 receptor antagonist, interleukin-6, monocyte chemotactic protein-1, soluble intercellular adhesion molecule-1,. . .

44. A method according to claim 43, wherein said marker of atherosclerotic plaque rupture is selected from the group consisting of human neutrophil elastase, inducible nitric oxide synthase, lysophosphatidic acid, malondialdehyde-modified low. . .

. . . of one or more markers selected from the group consisting of matrix metalloprotease-9 (MMP-9), an MMP-9-related marker, TpP, MCP-1, H-FABP, C-reactive protein, creatine kinase, MB isoenzyme, cardiac troponin I, cardiac troponin T, complexes comprising cardiac troponin I and cardiac troponin T, and B-type natriuretic protein in a sample obtained from said patient to said patient prognosis by determining if. . .

. . . according to claim 60, wherein said adverse outcome is selected from the group consisting of death, myocardial infarction, and congestive heart failure.

. . . of two or more markers selected from the group consisting of matrix metalloprotease-9 (MMP-9), an MMP-9-related marker, TpP, MCP-1, H-FABP, C-reactive protein, creatine kinase, MB isoenzyme, cardiac troponin I, cardiac troponin T, complexes comprising cardiac troponin I and cardiac troponin T, and B-type natriuretic protein in a sample obtained from

ANSWER 12 OF 1212 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:377301 BIOSIS
DOCUMENT NUMBER: PREV200100377301
TITLE: The effects of intravenous doxycycline therapy for rheumatoid arthritis: A randomized, double-blind, placebo-controlled trial.
AUTHOR(S): St.Clair, E. William [Reprint author]; Wilkinson, William E.; Pisetsky, David S.; Sexton, Daniel J.; Drew, Richard; Kraus, Virginia B.; Greenwald, Robert A.
CORPORATE SOURCE: Duke University Medical Center, Durham, NC, 27710, USA
SOURCE: Arthritis and Rheumatism, (May, 2001) Vol. 44, No. 5, pp. 1043-1047. print.
CODEN: ARHEAW. ISSN: 0004-3591.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 8 Aug 2001
Last Updated on STN: 19 Feb 2002

AB Objective: To determine the feasibility, safety, and potential clinical efficacy of intravenous (IV) doxycycline therapy for rheumatoid arthritis (RA), as well as its possible effects on serum and urinary markers of collagen breakdown. Methods: The exploratory trial was designed as a 16-week, single-center, randomized, double-blind, placebo-controlled trial. Eligible subjects with active seropositive or erosive RA were randomly allocated into 3 treatment groups: doxycycline 200 mg IV, azithromycin 250 mg orally, or placebo. The blinded IV study drug was administered once daily for the first 3 weeks by home self-infusion and then weekly for the next 8 weeks, concurrent with the blinded oral study drug at the prescribed doses. The primary end points were the change between baseline and week 4 in the tender joint count, erythrocyte sedimentation rate, and urinary excretion of pyridinoline. Results: The trial was stopped prematurely after enrollment of 31 patients. Three subjects were withdrawn because of worsening arthritis, and 1 patient was withdrawn when newly diagnosed with breast cancer. Infusion-related events occurred in 13 (42%) of 31 patients, but none were serious. There were 4 serious adverse events unrelated to the study drug, including a new diagnosis of breast cancer in 3 cases and hospitalization for abdominal pain in 1 case. No significant differences were observed across treatment groups in any of the 3 primary clinical end points. Conclusion: Although IV doxycycline therapy was generally well-tolerated by patients in this trial, it did not show any evidence of reducing disease activity or collagen crosslink production.

TI The effects of intravenous doxycycline therapy for rheumatoid arthritis: A randomized, double-blind, placebo-controlled trial.

SO Arthritis and Rheumatism, (May, 2001) Vol. 44, No. 5, pp. 1043-1047. print.
CODEN: ARHEAW. ISSN: 0004-3591.

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ANSWER 23 OF 1212 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2000:232964 BIOSIS
DOCUMENT NUMBER: PREV200000232964
TITLE: beta2-Microglobulin induces MMP-1 but not TIMP-1 expression in human synovial fibroblasts.
AUTHOR(S): Moe, Sharon M. [Reprint author]; Singh, Gurinder K. [Reprint author]; Bailey, Anna M. [Reprint author]
CORPORATE SOURCE: Division of Nephrology, Indiana University School of Medicine and Richard Roudebush Veterans Administration Medical Center, Indianapolis, IN, USA
SOURCE: Kidney International, (May, 2000) Vol. 57, No. 5, pp. 2023-2034. print.
CODEN: KDYIA5. ISSN: 0085-2538.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Jun 2000
Last Updated on STN: 5 Jan 2002

AB Background: beta2-Microglobulin (beta2m) amyloidosis is a destructive articular disease that causes significant morbidity in patients undergoing hemodialysis. The amyloid deposits contain beta2m, some of which is altered with advanced glycation end products (AGE-beta2m). The deposits are located principally in joint structures, with adjacent degradation of cartilage and bone. We hypothesized that one of the mechanisms by which beta2m induces joint destruction is to induce the release of matrix metalloproteinase-1 (MMP-1), but not tissue inhibitor of metalloproteinase-1 (TIMP-1), from synovial fibroblasts. Methods: To test this hypothesis and determine the role of AGE-beta2m, we incubated human osteoarthritic synovial fibroblasts in the presence and absence of beta2m and AGE-beta2m and measured the release of interstitial collagenase (MMP-1) and/or TIMP-1 by enzyme-linked immunosorbent assay and Northern blot analysis. Results: beta2m and AGE-beta2m at 10 and 25 mug/mL induced the release of MMP-1 from human osteoarthritic synovial fibroblasts at 24 hours. In contrast, there was no increased release of TIMP-1, leading to an increase in the MMP-1/TIMP-1 ratio indicative of uncontrolled collagenolysis. A similar dose response was observed at 48 hours, except that AGE-beta2m had no effect over control cultures. MMP-1 mRNA expression by Northern blot analysis paralleled these findings. The source of the fibroblasts did not alter the results. Finally, we demonstrated that doxycycline, a treatment for arthritis , can inhibit the release of MMP-1 from synovial fibroblasts incubated with beta2m. Conclusion: beta2m, at physiologically relevant concentrations, induces the release of MMP-1 without concomitant release of TIMP-1 from human synovial fibroblasts, leading to uncontrolled collagenolysis. The alteration of beta2m with AGE did not alter this effect at 24 hours, but blocked the effect at 48 hours. These findings may account for the tissue destruction seen in beta2m amyloidosis.
SO Kidney International, (May, 2000) Vol. 57, No. 5, pp. 2023-2034. print.
CODEN: KDYIA5. ISSN: 0085-2538.
AB. . . analysis paralleled these findings. The source of the fibroblasts did not alter the results. Finally, we demonstrated that doxycycline, a treatment for arthritis, can inhibit the release of MMP-1 from synovial fibroblasts incubated with beta2m. Conclusion: beta2m, at physiologically relevant concentrations, induces the. . .
RN 564-25-0 (doxycycline)
9001-12-1 (interstitial collagenase)
9001-12-1 (matrix metalloproteinase-1)
9001-12-1 (MMP-1)
140208-24-8 (tissue inhibitor of metalloproteinase-1)
140208-24-8 (TIMP-1)

ANSWER 15 OF 1212 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:5497 BIOSIS
DOCUMENT NUMBER: PREV200100005497
TITLE: Long-term treatment with subantimicrobial dose doxycycline exerts no antibacterial effect on the subgingival microflora associated with adult periodontitis.
AUTHOR(S): Walker, Clay [Reprint author]; Thomas, John; Nango, Sonia; Lennon, Jennifer; Wetzel, Jeanne; Powala, Christopher
CORPORATE SOURCE: Health Science Center, University of Florida, Gainesville, FL, 32610, USA
walkerc1@ufl.edu
SOURCE: Journal of Periodontology, (September, 2000) Vol. 71, No. 9, pp. 1465-1471. print.
CODEN: JOPRAJ. ISSN: 0022-3492.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Dec 2000
Last Updated on STN: 21 Dec 2000

AB Background: The purpose of this study was to determine whether treatment with subantimicrobial dose doxycycline (SDD), 20 mg bid, exerted an antimicrobial effect on the microflora associated with adult periodontitis. Methods: Following the approval of the protocol and informed consent forms by the respective IRBs at the University of Florida and West Virginia University, 76 subjects with adult periodontitis were entered and randomly assigned to receive SDD or placebo. A split-mouth design was utilized, with each subject receiving subgingival scaling and root planing (SRP) in two quadrants immediately following baseline data collection, while the remaining two quadrants were left unscaled (non-SRP). Microbial samples were collected prior to treatment, after 3, 6, and 9 months of treatment, and after 3 months of no treatment. The samples were examined by microscopy and by enumeration on selective and non-selective media. Results: All treatments resulted in statistically significant decreases in the proportions of spirochetes and motile rods ($P < 0.05$) and in an increase in the proportion of coccoid forms ($P < 0.0001$) relative to baseline. No between-treatment differences were detected between the SDD and placebo treatments in either the SRP or non-SRP design, with the exception of the small and large spirochetal groups. The spirochetal proportions present in the SDD group were significantly lower ($P < 0.05$) than the paired placebo group during the 9-month treatment and was preceded by a significant decrease ($P < 0.01$) in the proportion of microbiologic sample sites that bled on probing. No between-treatment differences were detected in any of the other microbial parameters. Conclusion: The microbial differences observed were attributed to the anticollagenase and anti-inflammatory properties of SDD and not to an antimicrobial effect.

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SO Journal of Periodontology, (September, 2000) Vol. 71, No. 9, pp. 1465-1471. print.
CODEN: JOPRAJ. ISSN: 0022-3492.

AB Background: The purpose of this study was to determine whether treatment with subantimicrobial dose doxycycline (SDD), 20 mg bid, exerted an antimicrobial effect on the microflora associated with adult periodontitis. Methods:. . . immediately following baseline data collection, while the remaining two quadrants were left unscaled (non-SRP). Microbial samples were collected prior to treatment, after 3, 6, and 9 months of treatment, and after 3 months of no treatment. The samples were examined by microscopy and by enumeration on selective and non-selective media. Results: All treatments resulted in statistically significant decreases in the proportions of spirochetes and motile rods ($P < 0.05$) and in an increase

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IT . . .
(Human Medicine, Medical Sciences); Pharmacology

IT Diseases
adult periodontitis: dental and oral disease

IT Chemicals & Biochemicals
doxycycline: anti-collagenase effect, anti-inflammatory effect, long-term treatment, subantimicrobial dose

RN 564-25-0 (doxycycline)